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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/790,658	03/01/2004	Cheryl D. Blume	SOM700/4-4CIP2CON2DIV	9575

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1615	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/790,658	BLUME ET AL.	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26 and 34-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26 and 34-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 8/9/07
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for rehearing dated 5-29-07 is acknowledged.

Claims 26 and 34-62 are pending in the instant application.

In view of the decision set forth by the Board of Appeals and Interferences dated 3-26-07, the finality of the rejection in the office action dated 5-17-05 has been withdrawn and the following new rejections have been applied to the instant claims:

Claim Rejections - 35 USC § 112

Claims 26 and 34-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Instant claims recite a method of treating "a condition" produced by immune system dysfunction that is associated with reduced levels of gamma-interferon production, comprising administering R(-) desmethylselegiline (DMS), wherein the administration leads to an increased production of gamma-interferon in the mammal. Instant claims are broad as they encompass a number of "conditions" that are stimulated or caused by immune dysfunction or immune deficiency.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: nature of the invention, breadth of the claims, state of the art, guidance of the specification, predictability if the art, and the working examples. All the factors

have been considered with regard to the claim, with the most relevant factors discussed below.

Nature of the Invention: All rejected claims are drawn to a method of treating "a condition" produced by immune system dysfunction that is associated with reduced levels of gamma-interferon production, comprising administering R(-) desmethylselegiline (DMS), wherein the administration leads to an increased production of gamma-interferon in the mammal. The nature of the invention is extremely complex in that it encompasses anticipating multiple complex diseases or disorders and subsequently administering the instant composition. The breadth of the claims exacerbates the complex nature of the claims. The claim encompasses treating complex disorders that may have potential causes other than those disclosed in the specification. The term immune dysfunction is not necessarily manifested by one condition i.e., pathogenesis, disease or disorder. For instance, AIDS (also described in the instant invention) is a complex of diseases and conditions, which are not necessarily treatable.

State of the Art: The state of the art does not recognize administration of the claimed compounds treat disorders such as substance abuse, neurological conditions associated with increased monoamine oxidase, reduced dopamine uptake etc. The state of the art however recognizes treating specific infections or diseases by administering gamma -interferon or other immunomodulating interleukins or chemokines. However, the functioning of immune system in response to an infection or a disease or disorder is modulated by not one immunomodualtor molecule but is a

complex interplay of several interleukins or chemokines. Further, a reduction in gamma-interferon does not necessarily result in immune system dysfunction. This is particularly evident from the cited references (Immunology, 1996 and Shi et al, J. Immunology 2004) in the case of AIDS, which applicants' claims as a condition caused by immune dysfunction and is associated with reduced gamma-interferon. Further, Billiau et al (also cited by applicants) studied the biological effects of gamma interferon under in vitro and in vivo conditions and observed that increased gamma-interferon did not always augment the immune system response (pages 76-81). It has been shown that HIV replication was in fact stimulated with gamma-interferon than being inhibited (page 96). This suggests that increasing the level of the above cytokine to treat AIDS (as in claims 37 and 60) would actually function in the opposite way i.e., enhance the AIDS condition, rather than providing a treatment. Billiau also shows that gamma-interferon increased the tumor growth, as opposed to the claimed treatment of cancer. On page 86, it is stated that the anti-viral effect of gamma-IFN is not expressed in mitogen-triggered primary T cells. Further, on page 89, gamma-IFN has been shown to mediate immune suppression as opposed to modulating or augmenting immune system. Billiau states that while gamma-IFN is generally assumed to play a role of in defense against bacteria and parasites, there is a general exception to the rule that endogenous IFN does not always provide the beneficial effect, as opposed to the exogenous IFN (page 95). Therefore, Billiau concludes that while the cytokine seemingly has beneficial effects, also has detrimental effects. Thus, the described or claimed (immune dysfunction) conditions may or may not be caused by gamma-interferon reduction or increasing the

levels of IFN-gamma may or may not yield positive results in the treatment of all the conditions related to reduced IFN-gamma levels.

Guidance of the Specification: The guidance given by the specification on how to treat the disorders is absent. Instant specification describes the effect of age on T cell function in terms of the levels of IL-2 and IFN-gamma. Further, the specification also describes the effect of DMS in restoring the levels of IL-2 and gamma-interferon. However, instant specification provides no guidance with respect to the procedure of administering instant composition to mammals for treating any or all of the disorders claimed. Instant specification also fails to provide any guidance or rationale showing that the claimed method is effective in completely treating any or all disorders produced by immune dysfunction, associated with reduced levels of gamma-IFN or to extrapolate the data provided to al immune dysfunction conditions, that are known to-date or yet to discovered.

Predictability of the Art & The Amount of Experimentation Necessary: The specification lacks guidance from the with regard to treating the claimed conditions, such that a completely effective treatment is ensured. Further, the state of the art recognizes that gamma-IFN levels need not necessarily be reduced in all immune dysfunction conditions or disorders and/or increased IFN-gamma need not always augment immune system function and thus treat the conditions associated with it. Thus, the lack of guidance from the specification together with unpredictability of reduced IFN levels in all immune dysfunctions (see above references), leads to further

unpredictability of the efficacy of DMS in treating conditions produced by immune system dysfuntion (associated with gamma-IFN). Therefore, the practitioner would turn to trial and error experimentation in order to determine the "conditions" caused by immune system dysfuntion (associated with gamma-IFN) in mammals that would respond to the claimed method of treatment (employing the claimed composition). Therefore, undue experimentation becomes the burden of the practitioner.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 26 and 34-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,387,615 to Milgram alone or Milgram in view of Borbe and Billiau.

Milgram describes the use of L-deprenyl for treating immune system dysfunction (abstract; col. 2, 11.60-64). L-deprenyl - also known as selegiline - is a selective monoamine oxidase B (MAO-B) inhibitor (col. 1, 11. 15-16). Immune system decline associated with aging is described as specific target for L-deprenyl therapy (col. 2, 11. 24-26; col. 2, 1.68 to col. 3, 1.4), which meets the conditions recited in claims 36 and 59. Milgram also describes that administration of L-deprenyl improves the immune response to an antigen (tetanus toxoid) challenge (col. 8-9, Example 8) and is hence of the same scope of claims 39 or

58 (vaccine or infectious diseases). Instant claims 39 and 62 cover this same indication. Milgram also shows that L-deprenyl improves T lymphocyte function (Example 2, cols. 7-8). AIDS is well known to be associated with T lymphocyte dysfunction. However, Milgram does not disclose the use of the claimed L-deprenyl metabolite, desmethyl-selegiline, to treat immune system dysfunction or to improve the immune response to an antigen.

Borbe teaches desmethylselegiline (DMS) and selegiline as effective MAO-B inhibitors, both of which irreversibly block MAO-B. Borbe also teaches oral administration of DMS in rats. Borbe does not specifically state that DMS is used for treating "a condition produced by immune system dysfunction that is associated with gamma-interferon production", as claimed. However, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ DMS of Borbe to treat the immune system dysfuntion related conditions associated with aging or to improve the immune system dysfunction because Borbe suggests that the activity of DMS is nearly equipotent to selegiline (L-deprenyl). The expected result is to improve immune system function and hence treat conditions associated with the same.

Although Milgram does not disclose that immune dysfunction in aging animals is associated with a decline in gamma-interferon as required by claim 26 and others, the disorders are the same. In view of the identity of the disorders, it would be reasonable to presume that immune system decline associated with aging, as taught by Milgram, would be accompanied by a reduction in gamma-interferon levels. Applicants also describe the effects of DMS treatment in increased IFN-gamma products in aged rats

(on page 40). While Milgram does not teach that L-deprenyl "leads to an increase in gamma-interferon production" as recited in claims, "[m] ere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention." *In re Baxter Travenol Labs.,* 952 F.2d 388, 392, 21 USPQ2d 1281, 1285 (Fed. Cir. 1991). *See also In re Woodruff,* 919 F.2d 1575, 1578, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990) ("It is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable."). In this case, the discovery that desmethyl-selegiline increases gamma-interferon product would be considered a latent property of an otherwise obvious process. This is further supported by the instant disclosure (page 40 of the instant specification) that IFN-gamma production is associated with IFN-gamma, as also described by Billiau. Therefore, a skilled artisan would have expected to see an increase in the IFN-gamma levels with the treatment of DMS of Borbe.

Examiner notes that applicants submitted a response to the decision rendered by the Board of Patent Appeals and Interferences. However, the response has been considered pre-mature, as it has been submitted before the examiner has taken an action. Therefore, the response has been held in abeyance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 7.00 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AU 1615
August 9, 2007

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